WEST Search History

DATE: Tuesday, September 09, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ			
L2	aureus and deformylase	46	L2
L1	aureus same deformylase	18	L1

END OF SEARCH HISTORY

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=> file .nash

=> s aureus and deformylase
L1          14 FILE MEDLINE
L2          36 FILE CAPLUS
L3          22 FILE SCISEARCH
L4           7 FILE LIFESCI
L5          38 FILE BIOSIS
L6          23 FILE EMBASE

TOTAL FOR ALL FILES
L7         140 AUREUS AND DEFORMYLASE

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8          77 DUP REM L7 (63 DUPLICATES REMOVED)

=> s l7 not 2002-2003/py
TOTAL FOR ALL FILES
L15         61 L7 NOT 2002-2003/PY

=> dup rem l15
PROCESSING COMPLETED FOR L15
L16         28 DUP REM L15 (33 DUPLICATES REMOVED)

=> d ibib abs 1-28

L16  ANSWER 1 OF 28     MEDLINE on STN                  DUPLICATE 1
ACCESSION NUMBER:   2001353916     MEDLINE
DOCUMENT NUMBER:    21140945   PubMed ID: 11246859
TITLE:              Backbone (1H, 15N, 13C) resonance assignments of a 21 kDa
                    construct of S. aureus peptide
                    deformylase.
AUTHOR:             Scahill T A; Kloosterman D A; Cialdella J I; Deibel M R Jr;
                    Marshall V P; Yem A W
SOURCE:             JOURNAL OF BIOMOLECULAR NMR, (2001 Jan) 19 (1) 81-2.
                    Journal code: 9110829. ISSN: 0925-2738.
PUB. COUNTRY:       Netherlands
DOCUMENT TYPE:      Letter
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200106
ENTRY DATE:         Entered STN: 20010625
                    Last Updated on STN: 20010625
                    Entered Medline: 20010621

L16  ANSWER 2 OF 28  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:        2001:453006  CAPLUS
DOCUMENT NUMBER:         135:61229
TITLE:                   Novel heterocyclic urea compounds, particularly
                         N-hydroxy-2-[N-substituted-N-[(2-substituted-
                         pyrrolidin-1-yl)carbonyl]amino]acetamides, with
                         activity as peptide deformylase inhibitors,
                         and their compositions, methods of use as
                         antimicrobials, and preparation
INVENTOR(S):             Ni, Zhi-jie; Jacobs, Jeffrey W.; Patel, Dinesh V.;
                         Lewis, Jason
PATENT ASSIGNEE(S):      Versicor, Inc., USA
SOURCE:                  PCT Int. Appl., 88 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  2
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.   DATE
     ---------------   ----  --------      ---------------   --------
     WO 2001044178      A1   20010621      WO 2000-US34126   20001213
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
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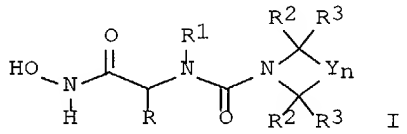
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 1999-466402 A1 19991217
OTHER SOURCE(S): MARPAT 135:61229
GI



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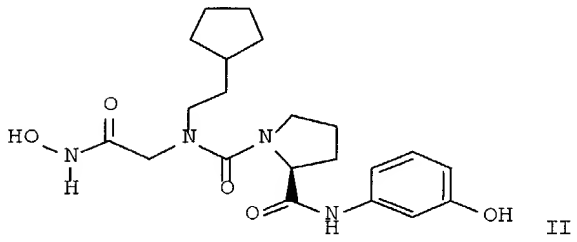

II

AB Novel hydroxamic acid compds. I are disclosed [wherein: R = H, R4, R5OH, R5OR6; R4, R6 = (un)substituted (hetero)alk(en/yn)yl or alkyl-(hetero)aryl-alkyl; R5 = (un)substituted (hetero)alk(en/yn)ylene or alkylene-(hetero)arylene-alkylene; R1 = H, (un)substituted (hetero)alk(en/yn)yl or alkyl-(hetero)aryl-alkyl; n = 1-5; zero or one Y group = O, NR7, or S; remaining Y = CR2R3; R2, R3 = H, R7, OH, OR7, SH, SR7, NH2, NHR7, NR7R8, COR7, CONR7R8, CO2R7, COCR7R8R9, CO2CR7R8R9, SO2NR7R8, etc.; R7, R8, R9 = H, (un)substituted (hetero)alk(en/yn)yl, alkoxy, or alkyl-(hetero)aryl-alkyl; or vicinal R2/R3 or vicinal pairs of R7/R8/R9 form (un)substituted cyclic (hetero)alkyl or (hetero)aryl group]. These hydroxamates inhibit peptide **deformylase** (PDF), an enzyme present in prokaryotes, and are therefore useful as antimicrobials and antibiotics. Methods of synthesis and use of the compds. are also disclosed. Over 60 synthetic examples are given. For instance, N-CBZ-L-proline was treated with SOCl2 and then 3-hydroxyaniline in pyridine to give the corresponding 3-hydroxyphenylamide, followed by deprotection of the proline N-terminus, coupling with N-[2-(cyclopentyl)ethyl]-N-[(methoxycarbonyl)methyl]carbamoyl chloride, and aminolysis with aq. NH2OH, to give title compd. II. Five std. formulations of I are described. I showed high selectivity for PDF over a variety of matrix and other metalloproteinases, and showed activity against Staphylococcus **aureus**, Staphylococcus epidermidis, Enterococcus faecium, Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, and Escherichia coli (no data).
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 28 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2001456719 MEDLINE
DOCUMENT NUMBER: 21393646 PubMed ID: 11502510
TITLE: Resistance of Streptococcus pneumoniae to **deformylase** inhibitors is due to mutations in defB.
AUTHOR: Margolis P; Hackbarth C; Lopez S; Maniar M; Wang W; Yuan Z;

White R; Trias J
CORPORATE SOURCE: Versicor, Inc., Fremont, California 94555, USA.
SOURCE: ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, (2001 Sep) 45 (9) 2432-5.
Journal code: 0315061. ISSN: 0066-4804.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20010815
Last Updated on STN: 20011008
Entered Medline: 20011004

AB Resistance to peptide **deformylase** inhibitors in Escherichia coli or Staphylococcus **aureus** is due to inactivation of transformylase activity. Knockout experiments in Streptococcus pneumoniae R6x indicate that the transformylase (fmt) and **deformylase** (defB) genes are essential and that a def paralog (defA) is not. Actinonin-resistant mutants of S. pneumoniae ATCC 49619 harbor mutations in defB but not in fmt. Reintroduction of the mutated defB gene into wild-type S. pneumoniae R6x recreates the resistance phenotype. The altered enzyme displays decreased sensitivity to actinonin.

L16 ANSWER 4 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:310657 BIOSIS
DOCUMENT NUMBER: PREV200200310657
TITLE: (Correction of Previews 200100340773. Identification of novel potent hydroxamic acid inhibitors of peptidyl **deformylase** and the importance of the hydroxamic acid functionality on inhibition. Correction of author name.
AUTHOR(S): Thorarensen, Atli (1); Deibel, Martin R., Jr.; Rohrer, Douglas C.; Vosters, Anne F.; Yem, Anthony W.; Marshall, Vincent D.; Lynn, Janet C.; Bohanon, Michael J.; Tomich, Paul K.; Zurenko, Gary E.; Sweeney, Michael T.; Jensen, Randy M.; Nielsen, James W.; Seest, Eric P.; Dolak, Lester A.
CORPORATE SOURCE: (1) Medicinal Chemistry, Pharmacia, 7254-209-615, Kalamazoo, MI, 49001-0199: atli.thorarensen@am.pnu.com USA
SOURCE: Bioorganic & Medicinal Chemistry Letters, (6 August, 2001) Vol. 11, No. 15, pp. 2053. http://www.elsevier.nl/inca/publications/store/9/7/2/. print.
ISSN: 0960-894X.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Regrettably, the author list as published contained an error. The correct list of authors reads as above.

L16 ANSWER 5 OF 28 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2002017802 MEDLINE
DOCUMENT NUMBER: 21322705 PubMed ID: 11429456
TITLE: YkrB is the main peptide **deformylase** in Bacillus subtilis, a eubacterium containing two functional peptide **deformylases**.
AUTHOR: Haas M; Beyer D; Gahlmann R; Freiberg C
CORPORATE SOURCE: Institute for Anti-infectives Research, Pharma Research, Bayer AG, D-42096 Wuppertal, Germany.
SOURCE: MICROBIOLOGY, (2001 Jul) 147 (Pt 7) 1783-91.
Journal code: 9430468. ISSN: 1350-0872.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20020121
Last Updated on STN: 20020121
Entered Medline: 20011204

AB Peptide deformylation is an essential process in eubacteria. The peptide **deformylase** Def has been suggested to be an attractive target for antibacterial drug discovery. Some eubacteria including medically important pathogens possess two def-like genes. Until now, the

functionality of both genes has been tested only in Staphylococcus **aureus** with the result that one gene copy was functional. Here, expression of two functional def-like gene products in Bacillus subtilis is demonstrated. Besides the def gene, which is chromosomally located close to the formyltransferase gene fmt and which was overexpressed and biochemically tested previously, B. subtilis possesses a second def-like gene, called ykrB. The encoded protein is 32% identical to the def gene product. It was shown that either def or ykrB had to be present for growth of B. subtilis in rich medium (each was individually dispensable). Studies with a def/ykrB double deletion strain with xylose-inducible ykrB copy demonstrated that, besides def, the gene ykrB is a second cellular target of **deformylase** inhibitors such as the antibiotic actinonin. The gene products exhibited similar enzymic properties, exemplified by similar inhibition efficacy of actinonin in biochemical assays. Antibiotic susceptibility tests with different deletion strains and Northern analyses indicated that YkrB is probably the predominant **deformylase** in B. subtilis. It was shown that duplication of the **deformylase** function does not lead to an increased actinonin-resistance frequency in comparison to B. subtilis mutants carrying only one **deformylase** gene.

L16 ANSWER 6 OF 28 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2001297107 MEDLINE
DOCUMENT NUMBER: 21271840 PubMed ID: 11378353
TITLE: Identification of novel potent hydroxamic acid inhibitors of peptidyl **deformylase** and the importance of the hydroxamic acid functionality on inhibition.
COMMENT: Erratum in: Bioorg Med Chem Lett 2001 Aug 6;11(15):2053
AUTHOR: Thorarensen A; Deibel M R Jr; Rohrer D C; Vosters A F; Yem A W; Marshall V D; Lynn J C; Bohanon M J; Tomich P K; Zurenko G E; Sweeney M T; Jensen R M; Nielsen J W; Seest E P; Dolak L A
CORPORATE SOURCE: Medicinal Chemistry 7254-209-615, Pharmacia, Kalamazoo, MI 49001-0199, USA.. atli.thorarensen@am.pnu.com
SOURCE: BIOORGANIC AND MEDICINAL CHEMISTRY LETTERS, (2001 Jun 4) 11 (11) 1355-8.
Journal code: 9107377. ISSN: 0960-894X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010910
Last Updated on STN: 20011003
Entered Medline: 20010906

AB Peptidyl **deformylase** (PDF) is a metallo protease that catalyzes the removal of a formyl group from the N-termini of prokaryotic prepared polypeptides, an essential step in bacterial protein synthesis. Screening of our compound collection using Staphylococcus **aureus** PDF afforded a very potent inhibitor with an IC(50) in the low nanomolar range. Unfortunately, the compound that contains a hydroxamic acid did not exhibit antibacterial activity (MIC). In order to address the lack of activity in the MIC assay and to determine what portion of the molecule was responsible for binding to PDF, we prepared several analogues. This paper describes our findings that the hydroxamic acid functionality found in 1 is mainly responsible for the high affinity to PDF. In addition, we identified an alternative class of PDF inhibitors, the N-hydroxy urea 18, which has both PDF and antibacterial activity.

L16 ANSWER 7 OF 28 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2001:999241 SCISEARCH
THE GENUINE ARTICLE: 500TJ
TITLE: Exploiting genomics to discover new antibiotics
AUTHOR: McDevitt D (Reprint); Rosenberg M
CORPORATE SOURCE: GlaxoSmithKline, Antimicrobials & Host Def CEDD, Collegeville, PA 19426 USA (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: TRENDS IN MICROBIOLOGY, (DEC 2001) Vol. 9, No. 12, pp. 611-617.
Publisher: ELSEVIER SCIENCE LONDON, 84 THEOBALDS RD, LONDON WC1X 8RR, ENGLAND.

ISSN: 0966-842X.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 60
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB There is an urgent need to develop new classes of antibiotics to tackle the increase in resistance in many common bacterial pathogens. One strategy to develop new antibiotics is to identify and exploit new molecular targets and this strategy is being driven by the wealth of new genome sequence information now available. Additionally, new technologies have been developed to validate new antibacterial targets, for example, new technologies have been developed to enable rapid determination of whether a gene is essential and to assess the transcription status of a putative target during infection. As a result, many novel validated targets have now been identified and for some, appropriate high-throughput screens against diverse compound collections have been carried out. Novel antibiotic leads are emerging from these genomics-derived targeted screens and the challenge now is to optimize and develop these leads to become part of the next generation of antibiotics.

L16 ANSWER 8 OF 28 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001167167 MEDLINE
DOCUMENT NUMBER: 21091832 PubMed ID: 11158755
TITLE: Antibiotic activity and characterization of BB-3497, a novel peptide **deformylase** inhibitor.
AUTHOR: Clements J M; Beckett R P; Brown A; Catlin G; Lobell M; Palan S; Thomas W; Whittaker M; Wood S; Salama S; Baker P J; Rodgers H F; Barynin V; Rice D W; Hunter M G
CORPORATE SOURCE: British Biotech Pharmaceuticals Ltd., Oxford OX4 6LY, United Kingdom.. clements@britbio.co.uk
SOURCE: ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, (2001 Feb) 45 (2) 563-70.
Journal code: 0315061. ISSN: 0066-4804.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1G27; PDB-1G2A
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010510

AB Peptide **deformylase** (PDF) is an essential bacterial metalloenzyme which deformylates the N-formylmethionine of newly synthesized polypeptides and as such represents a novel target for antibacterial chemotherapy. To identify novel PDF inhibitors, we screened a metalloenzyme inhibitor library and identified an N-formyl-hydroxylamine derivative, BB-3497, and a related natural hydroxamic acid antibiotic, actinonin, as potent and selective inhibitors of PDF. To elucidate the interactions that contribute to the binding affinity of these inhibitors, we determined the crystal structures of BB-3497 and actinonin bound to Escherichia coli PDF at resolutions of 2.1 and 1.75 A, respectively. In both complexes, the active-site metal atom was pentacoordinated by the side chains of Cys 90, His 132, and His 136 and the two oxygen atoms of N-formyl-hydroxylamine or hydroxamate. BB-3497 had activity against gram-positive bacteria, including methicillin-resistant Staphylococcus **aureus** and vancomycin-resistant Enterococcus faecalis, and activity against some gram-negative bacteria. Time-kill analysis showed that the mode of action of BB-3497 was primarily bacteriostatic. The mechanism of resistance was via mutations within the formyltransferase gene, as previously described for actinonin. While actinonin and its derivatives have not been used clinically because of their poor pharmacokinetic properties, BB-3497 was shown to be orally bioavailable. A single oral dose of BB-3497 given 1 h after intraperitoneal injection of S. **aureus** Smith or methicillin-resistant S. **aureus** protected mice from infection with median effective doses of 8 and 14 mg/kg of body weight, respectively. These data validate PDF as a novel target for the design of a new generation of antibacterial agents.

L16 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:640926 CAPLUS

TITLE: Structure-based design of inhibitors to peptide **deformylase** for use as anti-bacterial agents
AUTHOR(S): Hruza, Alan
CORPORATE SOURCE: Structural Chemistry, Schering Plough Research Institute, Kenilworth, NJ, 07033, USA
SOURCE: Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26-30, 2001 (2001), ORGN-563. American Chemical Society: Washington, D. C.
CODEN: 69BUZP
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB In prokaryotes, a formylated methionine is the first residue of newly synthesized polypeptides. Several essential proteins require the removal of the N terminal formyl group to be active; hence this step is required for bacterial survival. Deformylation is performed by peptide **deformylase** (Pdf), a common bacterial enzyme. Eukaryotes do not have an enzyme equiv. to Pdf, making it an attractive target for the development of anti-infectious agents. To support structure-based design of inhibitors to Pdf; we have crystd. the biol. relevant iron contg. form of Pdf. Improvements to the published purifn. protocols produced crystals of both Escherichia coli and Staphylococcus **aureus** enzymes. Crystals of both enzymes diffract to high resoln. (1.6 .ANG. or greater). Mol. replacement attempts with the E. coli Pdf structure to solve the S. **aureus** Pdf failed, using conventional techniques. By combining the max. likelihood target (BUSTER) and automated refinement procedure (ARP/WARP) the structure was solved. The current structure of S. **aureus** Pdf has an Rwork=18.6% and Rfree of 21.8% at 1.6 .ANG.. The first Pdf inhibitor lead discovered by whole-cell assay screening was actinonin. Actinonin is a hydroxamate contg. natural product. The X-ray structure of the E. coli Pdf-actinonin complex at 1.5 .ANG. was our initial template for a structure-based design program of Pdf inhibitors. Eighteen E. coli Pdf-inhibitor complexes and ligand free structures of E. coli and S. **aureus** Pdf have been detd. In our current best inhibitor, the hydroxamate group is replaced by a carboxylate, while still maintaining low nanomolar inhibition. Structural comparison of the active sites from both species of Pdf shows significant similarities. This study provides the background at a mol. level for the structure-based design of a broad-spectrum antibiotic against Pdf.

L16 ANSWER 10 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:555352 BIOSIS
DOCUMENT NUMBER: PREV200200555352
TITLE: Iterative parallel synthesis-derived N-alkyl urea hydroxamic acids: A new class of peptide **deformylase** inhibitors.
AUTHOR(S): Lewis, J. G. (1); Jacobs, J. (1); Wu, C. (1); Hackbarth, C. (1); Wang, W. (1); Lopez, S. (1); White, R. (1); Trias, J. (1); Yuan, Z. (1); Patel, D. V. (1)
CORPORATE SOURCE: (1) Versicor, Inc., Fremont, CA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2001) Vol. 41, pp. 207. print. Meeting Info.: 41st Annual Meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy Chicago, Illinois, USA September 22-25, 2001
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Peptide **deformylase** (PDF) is a prokaryotic metalloenzyme essential for bacterial growth. Previously, actinonin was identified as a potent PDF inhibitor (Chen, et al, (2000) Biochemistry 39) and studies with a series of hydroxamate alkylsuccinate validated the enzyme as a target for development of antibacterial agents (40th ICAAC, Poster 2173, 2174, and 2175). The urea core pharmacophore was envisioned as a constrained carbonyl isostere of the alkylsuccinate backbone. VRC3852, the initial lead that incorporated the urea core, was identified as an inhibitor of E. coli Ni2+ PDF with an IC50 of 11 nM. While VRC3852 represents a structurally distinct class of PDF inhibitor, the compound has moderate antibacterial activity against S. **aureus** (MICs 4-16 mug/ml) and S. pneumoniae (MICs 16-32 mug/ml). A synthetic sequence amenable to solid phase synthesis was developed and diverse chemical functionality was incorporated into the urea core structure to facilitate

its binding to S1 and S2+S3 sites of the enzyme. Using VRC3852 as an initial lead, the antibacterial spectrum and potency of this series of N-alkyl urea hydroxamic acids, together with their other important pharmaceutical properties, were optimized through three rounds of iterative parallel synthesis. Each compound was evaluated for its antibacterial activity against a panel of Gram (+) and Gram (-) pathogens together with its ability to inhibit PDF activity. The results of these biological evaluations were used to guide analog selection in subsequent rounds of parallel synthesis. This process identified several N-alkyl urea hydroxamic acids with MIC ltoreql mug/ml against S. **aureus**, S. pneumonia, and H. influenzae.

L16 ANSWER 11 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:555351 BIOSIS
DOCUMENT NUMBER: PREV200200555351
TITLE: Preclinical analysis of N-alkyl urea hydroxamic acid peptide **deformylase** inhibitors.
AUTHOR(S): Chen, D. (1); Clark, K.; Cramer, J.; Mangold, J.; Koehn, J.; Lewis, J. G. (1); Hackbarth, C. (1); Wu, C. (1); Wang, W. (1); Lopez, S. (1); Wither, G. (1); Gu, H.; Dunn, E.; Kulathila, R.; Porter, W.; Weidmann, B.; Patel, D. V. (1); White, R. J. (1); Trias, J. (1); Yuan, Z. (1)
CORPORATE SOURCE: (1) Versicor, Inc., Fremont, CA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2001) Vol. 41, pp. 207. print.
Meeting Info.: 41st Annual Meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy Chicago, Illinois, USA September 22-25, 2001
DOCUMENT TYPE: Conference
LANGUAGE: English
AB N-alkyl urea hydroxamic acids were identified at Versicor as potent PDF inhibitors with structural novelty. Two of the lead compounds, VRC4232 and VRC4307, were discovered through an integrated combinatorial and medicinal chemistry approach. VRC4307 inhibits PDF enzymes from both Gram (+) and Gram (-) bacteria with Ki <2 muM against Ni2+-enzyme from E. coli, and has excellent antibacterial activity. The bacterial PDF was co-crystallized with VRC4307, and the enzyme-inhibitor structure was determined at 1.7ANG resolution. This structural information indicates that the urea compounds adopt a binding position similar to the one previously determined for succinate hydroxamates. The in vivo efficacy of both compounds was determined using a S. **aureus** (Smith strain) septicemia model in mice. Both VRC4232 and VRC4307 are effective via subcutaneous administration with 50% protective dose (PD50) of 30.8 and 17.9 mg/kg, respectively. Following a single i.v. injection, the clearance rate of VRC4232 and VRC4307 was determined in mice with terminal t1/2 of 1.1 and 0.1 hr, respectively. In an in vitro metabolic stability assay, although both compounds were rapidly metabolized by mouse and rat liver microsomes, they are very stable in human liver microsomes. The in vivo- and in vitro-derived metabolites were analyzed and one of the major metabolic liabilities is the modification of the hydroxamic acid moiety. In summary, structurally novel urea based PDF inhibitors with antibacterial activity were identified and evaluated in vivo. Based on the efficacy and pharmacokinetic studies, lead compounds of N-alkyl urea hydroxamic acids may provide a starting point for the discovery of a new class of PDF inhibitors as antimicrobial agents.

L16 ANSWER 12 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:555350 BIOSIS
DOCUMENT NUMBER: PREV200200555350
TITLE: In vitro profile of N-alkyl urea hydroxamic acids that inhibit bacterial peptide **deformylase**.
AUTHOR(S): Hackbarth, C. (1); Lopez, S. (1); Lewis, J. G. (1); Wu, C. (1); Wang, W. (1); Wither, G. (1); Chen, D. (1); Jacobs, J. (1); Patel, D. V. (1); White, R. J. (1); Trias, J. (1); Yuan, Z. (1)
CORPORATE SOURCE: (1) Versicor, Inc., Fremont, CA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2001) Vol. 41, pp. 206-207. print.
Meeting Info.: 41st Annual Meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy

Chicago, Illinois, USA September 22-25, 2001
DOCUMENT TYPE: Conference
LANGUAGE: English
AB N-alkyl urea hydroxamic acids have recently been shown to inhibit the activity of peptide **deformylase**, a bacterial metalloprotease. Using iterative parallel synthesis, three combinatorial libraries were constructed and screened for enzymatic and antibacterial activity. Several compounds achieved MICs ltoreq4 mug/ml against Gram positive and Gram negative pathogens, including Staphylococcus **aureus**, Streptococcus pneumoniae and Haemophilus influenzae. The IC50s vs Escherichia coli Ni++-PDF were ltoreq0.1 muM denoting the specificity of the inhibitors. In addition, the IC50s were consistently >200 muM against matrilysin, a member of the matrix metalloprotease superfamily, and other mammalian metalloproteases. These data suggest N-alkyl urea hydroxamic acid compounds are selective for bacterial rather than mammalian metalloproteases. As with the succinate hydroxamates PDF inhibitors, this class of compounds is bacteriostatic against S. pneumoniae and H. influenzae and resistant mutants are selected in vitro at a frequency of 10-8. Structure activity relationship analysis identified preferred substitutions resulting in improved potency and decreased cytotoxity. We have identified VRC4232 and VRC4307 as promising leads for this new class of PDF inhibitors.

L16 ANSWER 13 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:555346 BIOSIS
DOCUMENT NUMBER: PREV200200555346
TITLE: In vitro activity of BB 83698 and two other peptide **deformylase** inhibitors compared to ciprofloxacin, moxfloxacin, gentamicin and linezolid against heterogeneous glycopeptide intermediate Staphylococcus **aureus** (hGISA) and GISA.
AUTHOR(S): Wootton, M. (1); Howe, R. A. (1); MacGowan, A. P. (1); Walsh, T. R.; Bennett, P. M.
CORPORATE SOURCE: (1) BCARE, Bristol UK
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2001) Vol. 41, pp. 206. print. Meeting Info.: 41st Annual Meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy Chicago, Illinois, USA September 22-25, 2001
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Background: BB 83698, BB 84234 and BB 84518 are representatives of a new class of peptide **deformylase** inhibitor (PDI) undergoing clinical evaluation. These compounds have in-vitro activity against Gram-positive and Gram-negative bacteria. GISA and hGISA have been reported in many countries world-wide and are likely to present the next important challenge for any new drug class with significant anti Gram-positive activity. It is therefore important to evaluate agents of a new class against these pathogens. Methods: Using NCCLS methods the in-vitro potency of the three PDIs (BB 83698, BB 84234 and BB 84518) and four comparators gentamicin (GEN), moxifloxacin (MOX), ciprofloxacin (CIP) and linezolid (LIN) were assessed against hGISA 9n=33) and GISA (n=10) strains isolated in the US, Japan and Europe. MICs were read at 24h. Results: MICs are given. Conclusions: GEN and CIP have poor in-vitro potency against these strains. MOX is markedly more potent than CIP but LIN has the lowest MIC50/MIC90 values of the comparators. BB 83698 and BB 84234 have similar potency but BB 84518 was 2-4 fold more active with MIC50 of 0.5-1 mg/L. These peptide **deformylase** inhibitors have potent in-vitro activity against GISA and hGISA.

L16 ANSWER 14 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:555347 BIOSIS
DOCUMENT NUMBER: PREV200200555347
TITLE: In vitro activity of peptide **deformylase** inhibitors, a new class of antimicrobials, against Gram-positive pathogens.
AUTHOR(S): Wise, R. (1)
CORPORATE SOURCE: (1) City Hospital, Birmingham UK
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2001) Vol. 41, pp. 206. print. Meeting Info.: 41st Annual Meeting of the Interscience

Conference on Antimicrobial Agents and Chemotherapy
Chicago, Illinois, USA September 22-25, 2001
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Background: Peptide **deformylase** (PDF) is an essential bacterial metalloenzyme that deformylates the N-formylmethionine of newly synthesized bacterial polypeptides, and as such represents a novel target for antimicrobial chemotherapy. Methods: The in vitro activity of a series of PDF inhibitors was compared with that of ciprofloxacin, co-amoxiclav, and linezolid against 40 Streptococcus pneumoniae (including strains resistant to penicillin and laboratory mutants with high-level quinolone resistance), 20 Group A streptococci, 30 methicillin-susceptible Staphylococcus **aureus** (MSSA) and 20 methicillin-resistant S. **aureus** (MRSA). MICs were determined on Iso-Sensitest Agar supplemented with 5% defibrinated horse blood and 20 mg/L NAD. The inoculun was 104 cfu/spot. Plates were incubated for 18-20 h in air (fastidious organisms supplemented with 4-6% CO2). Results: Susceptibility results are given (mg/L). Conclusions: This series of PDF inhibitors showed good in vitro activity against the major Gram-positive respiratory pathogens, including quinolone- and penicillin-resistant pneumococci and MRSA. These data suggest that PDF inhibitors are a promising new class of antimicrobials with potential for the treatment of respiratory tract infections.

L16 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:639947 CAPLUS
TITLE: Use of simple parallel synthesis to improve the antibacterial activity of .alpha.-aminoacetamides
AUTHOR(S): Thorarensen, Atli; Rohrer, Douglas; Zurenko, Gary; Sweeney, Michael
CORPORATE SOURCE: Medicinal Chemistry, 7254-209-615, Pharmacia, Kalamazoo, MI, 49007-494, USA
SOURCE: Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26-30, 2001 (2001), MEDI-128. American Chemical Society: Washington, D. C.
CODEN: 69BUZP
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Antibacterial resistance to a range of available antibiotics is a problem in the treatment of bacterial infections. Current efforts at Pharmacia have relied on a combination of genomics for the identification of novel mechanistic targets essential for bacterial survival and the identification of compds. with whole cell activity against the microorganism Staphylococcus **aureus**. These assays are currently utilized for the screening of our Research Compd. Collection. Screening of our compd. collection with S. **aureus** peptidyl **deformylase** afforded a very potent inhibitor with IC50 in the low nM range. Unfortunately the compd. did not have any antibacterial activity (MIC). During our attempts to design and prep. compds. with antibacterial and peptidyl **deformylase** activity we discovered the .alpha.-aminoacetamide 1. The .alpha.-aminoacetamide 1 had very modest antibacterial activity but was devoid of peptidyl **deformylase** activity. The structural simplicity, combined with an interesting structural motif prompted us to explore this lead utilizing parallel synthesis. This poster will describe our effort in this area and the discovery of 2 which has greatly improved activity compared to the activity of 1.

L16 ANSWER 16 OF 28 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2001:896087 SCISEARCH
THE GENUINE ARTICLE: BT13H
TITLE: Chapter 9. Recent developments in antibacterial research
AUTHOR: Bronson J J (Reprint); Barrett J F
CORPORATE SOURCE: Bristol Myers Squibb Co, Pharmaceut Res Inst, 5 Res Pkwy, Wallingford, CT 06492 USA (Reprint); Bristol Myers Squibb Co, Pharmaceut Res Inst, Wallingford, CT 06492 USA
COUNTRY OF AUTHOR: USA
SOURCE: ANNUAL REPORTS IN MEDICINAL CHEMISTRY, VOL 36, (DEC 2001) Vol. 36, pp. 89-98.
Publisher: ACADEMIC PRESS INC, 525 B STREET, SUITE 1900,

SAN DIEGO, CA 92101-4495 USA.
ISSN: 0065-7743.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 133

L16 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2001:159959 CAPLUS
DOCUMENT NUMBER: 134:337561
TITLE: Backbone (1H, 15N, 13C) resonance assignments of a 21 kDa construct of S. **aureus** peptide **deformylase**
AUTHOR(S): Scahill, Terrence A.; Kloosterman, David A.; Cialdella, Joyce I.; Deibel, Martin R., Jr.; Marshall, Vincent P.; Yem, Anthony W.
CORPORATE SOURCE: Structural, Analytical & Medicinal Chemistry Research, Pharmacia Corp., St, Kalamazoo, MI, 49001-0199, USA
SOURCE: Journal of Biomolecular NMR (2001), 19(1), 81-82
CODEN: JBNME9; ISSN: 0925-2738
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Peptide **deformylase** is a metallopeptidase which uses iron as a catalytic metal for amide hydrolysis. Potent inhibitors of Staphylococcus **aureus** peptide **deformylase** could selectively block growth of bacterial cells with the benefit of low toxicity in humans. This makes peptide **deformylase** an attractive target for structure-based drug design of potent inhibitors once the NMR resonance assignments are made and the secondary and tertiary structure is detd. Here we report the backbone 1H, 15 N and 13C.alpha., 13C.beta., and 13C' assignments of the zinc form of S. **aureus** peptide **deformylase**.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 18 OF 28 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2000416795 MEDLINE
DOCUMENT NUMBER: 20316793 PubMed ID: 10858337
TITLE: Peptide **deformylase** in Staphylococcus **aureus**: resistance to inhibition is mediated by mutations in the formyltransferase gene.
AUTHOR: Margolis P S; Hackbarth C J; Young D C; Wang W; Chen D; Yuan Z; White R; Trias J
CORPORATE SOURCE: Versicor, Inc., Fremont, California 94555, USA.
SOURCE: ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, (2000 Jul) 44 (7) 1825-31.
Journal code: 0315061. ISSN: 0066-4804.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000907
Last Updated on STN: 20000907
Entered Medline: 20000831
AB Peptide **deformylase**, a bacterial enzyme, represents a novel target for antibiotic discovery. Two **deformylase** homologs, defA and defB, were identified in Staphylococcus **aureus**. The defA homolog, located upstream of the transformylase gene, was identified by genomic analysis and was cloned from chromosomal DNA by PCR. A distinct homolog, defB, was cloned from an S. **aureus** genomic library by complementation of the arabinose-dependent phenotype of a P(BAD)-def Escherichia coli strain grown under arabinose-limiting conditions. Overexpression in E. coli of defB, but not defA, correlated to increased **deformylase** activity and decreased susceptibility to actinonin, a **deformylase**-specific inhibitor. The defB gene could not be disrupted in wild-type S. **aureus**, suggesting that this gene, which encodes a functional **deformylase**, is essential. In contrast, the defA gene could be inactivated; the function of this gene is unknown. Actinonin-resistant mutants grew slowly in vitro and did not show cross-resistance to other classes of antibiotics. When compared to

the parent, an actinonin-resistant strain produced an attenuated infection in a murine abscess model, indicating that this strain also has a growth disadvantage in vivo. Sequence analysis of the actinonin-resistant mutants revealed that each harbors a loss-of-function mutation in the fmt gene. Susceptibility to actinonin was restored when the wild-type fmt gene was introduced into these mutant strains. An S. **aureus** Deltafmt strain was also resistant to actinonin, suggesting that a functional **deformylase** activity is not required in a strain that lacks formyltransferase activity. Accordingly, the defB gene could be disrupted in an fmt mutant.

L16 ANSWER 19 OF 28 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2000150397 MEDLINE
DOCUMENT NUMBER: 20150397 PubMed ID: 10684604
TITLE: Actinonin, a naturally occurring antibacterial agent, is a potent **deformylase** inhibitor.
AUTHOR: Chen D Z; Patel D V; Hackbarth C J; Wang W; Dreyer G; Young D C; Margolis P S; Wu C; Ni Z J; Trias J; White R J; Yuan Z
CORPORATE SOURCE: Versicor, Inc., Fremont, California 94555, USA.
SOURCE: BIOCHEMISTRY, (2000 Feb 15) 39 (6) 1256-62.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000327
Last Updated on STN: 20000327
Entered Medline: 20000313
AB Peptide **deformylase** (PDF) is essential in prokaryotes and absent in mammalian cells, thus making it an attractive target for the discovery of novel antibiotics. We have identified actinonin, a naturally occurring antibacterial agent, as a potent PDF inhibitor. The dissociation constant for this compound was 0.3 x 10(-)(9) M against Ni-PDF from Escherichia coli; the PDF from Staphylococcus **aureus** gave a similar value. Microbiological evaluation revealed that actinonin is a bacteriostatic agent with activity against Gram-positive and fastidious Gram-negative microorganisms. The PDF gene, def, was placed under control of P(BAD) in E. coli tolC, permitting regulation of PDF expression levels in the cell by varying the external arabinose concentration. The susceptibility of this strain to actinonin increases with decreased levels of PDF expression, indicating that actinonin inhibits bacterial growth by targeting this enzyme. Actinonin provides an excellent starting point from which to derive a more potent PDF inhibitor that has a broader spectrum of antibacterial activity.

L16 ANSWER 20 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 9
ACCESSION NUMBER: 2000:697883 CAPLUS
DOCUMENT NUMBER: 134:276406
TITLE: Regulated gene expression in Staphylococcus **aureus** for identifying conditional lethal phenotypes and antibiotic mode of action
AUTHOR(S): Zhang, L.; Fan, F.; Palmer, L. M.; Lonetto, M. A.; Petit, C.; Voelker, L. L.; St. John, A.; Bankosky, B.; Rosenberg, M.; McDevitt, D.
CORPORATE SOURCE: Anti-Infectives Research, SmithKline Beecham Pharmaceuticals Research and Development, Collegeville, PA, 19426, USA
SOURCE: Gene (2000), 255(2), 297-305
CODEN: GENED6; ISSN: 0378-1119
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Selectively regulating gene expression in bacteria has provided an important tool for studying gene function. However, well-regulated gene control systems have been restricted primarily for use in lab. non-pathogenic strains of bacteria e.g. Escherichia coli, Bacillus subtilis. The development of analogous systems for use in bacterial pathogens such as Staphylococcus **aureus** would significantly enhance our ability to examine the contribution of any given gene product to pathogen growth and viability. In this report, we adapt, examine and

compare three regulated gene expression systems in S. **aureus**, which had previously been used in B. subtilis. We demonstrate that all three systems function and exhibit titratable induction, together covering a dynamic range of gene expression of .apprx.3000-fold. This dynamic range correlates well with the physiol. expression levels of cellular proteins. Importantly, we show that one of these systems, the Spac system, is particularly useful for examg. gene essentiality and creating specific conditional lethal phenotypes. Moreover, we find that titrn. of selective target gene products using this system allows direct demonstration of antibiotic mode of action.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 21 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:543633 BIOSIS
DOCUMENT NUMBER: PREV200000543633
TITLE: In vivo evaluation of VRC3375, a potent peptide **deformylase** inhibitor.
AUTHOR(S): Chen, D. (1); Hackbarth, C. (1); Ni, Z. J. (1); Wang, W. (1); Wu, C. (1); Young, D. (1); White, R. J. (1); Trias, J. (1); Patel, D. V. (1); Yuan, Z. (1)
CORPORATE SOURCE: (1) Versicor, Inc., Fremont, CA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2000) Vol. 40, pp. 228. print. Meeting Info.: 40th Interscience Conference on Antimicrobial Agents and Chemotherapy Toronto, Ontario, Canada September 17-20, 2000
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L16 ANSWER 22 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:543631 BIOSIS
DOCUMENT NUMBER: PREV200000543631
TITLE: Microbiological and enzymatic evaluation of **deformylase** inhibitors.
AUTHOR(S): Hackbarth, C. (1); Lopez, S. (1); Wang, W. (1); Jacobs, J. (1); Jacobs, J. (1); Jain, R. (1); Ni, Z. J. (1); Trias, J. (1); Chen, D. (1); Withers, G. (1); Patel, D. V. (1); Yuan, Z. (1)
CORPORATE SOURCE: (1) Versicor, Inc., Fremont, CA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2000) Vol. 40, pp. 228. print. Meeting Info.: 40th Interscience Conference on Antimicrobial Agents and Chemotherapy Toronto, Ontario, Canada September 17-20, 2000
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L16 ANSWER 23 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:543634 BIOSIS
DOCUMENT NUMBER: PREV200000543634
TITLE: Discovery and in vitro enzyme activity of BB-3497, a new class of peptide **deformylase** inhibitor.
AUTHOR(S): Thomas, W. (1); Beckett, P. (1); Chandler, S. (1); Clements, J. M. (1); Catlin, G. (1); Galloway, W. A. (1); Hunter, M. G. (1)
CORPORATE SOURCE: (1) British Biotech Pharmaceuticals Ltd., Oxford UK
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2000) Vol. 40, pp. 228. print. Meeting Info.: 40th Interscience Conference on Antimicrobial Agents and Chemotherapy Toronto, Ontario, Canada September 17-20, 2000
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L16 ANSWER 24 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:543632 BIOSIS
DOCUMENT NUMBER: PREV200000543632

TITLE: Distinct mechanisms of resistance to **deformylase** inhibitors in Haemophilus influenzae and Streptococcus pneumoniae.
AUTHOR(S): Margolis, P. (1); Hackbarth, C. (1); Maniar, M. (1); Lopez, S. (1); White, R. (1); Yuan, Z. (1); Trias, J. (1)
CORPORATE SOURCE: (1) Versicor, Inc., Fremont, CA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2000) Vol. 40, pp. 228. print. Meeting Info.: 40th Interscience Conference on Antimicrobial Agents and Chemotherapy Toronto, Ontario, Canada September 17-20, 2000
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L16 ANSWER 25 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:723015 CAPLUS
DOCUMENT NUMBER: 131:322926
TITLE: Methods for solid-phase synthesis of hydroxylamine compounds and derivatives and combinatorial libraries
INVENTOR(S): Patel, Dinesh V.; Ngu, Khehyong
PATENT ASSIGNEE(S): Versicor, Inc., USA
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9957097	A2	19991111	WO 1999-US9996	19990506
WO 9957097	A3	20000309		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6281245	B1	20010828	US 1998-74035	19980506
AU 9939748	A1	19991123	AU 1999-39748	19990506

PRIORITY APPLN. INFO.:

US 1998-74035	A	19980506
US 1996-29788P	P	19961028
US 1997-47468P	P	19970523
US 1997-958638	A2	19971027
WO 1999-US9996	W	19990506

OTHER SOURCE(S): MARPAT 131:322926
AB Hydroxylamine compds. HONHCOCH2CH(CH2CH2-X-Me)CO-L10-CO-R2 [X = CH2, S; L10 = NHCHMe, NHCH(Bu-i), NHCH(CH2)Ph and related residues of optically active amino acids; R2 = NH2, piperidino, morpholino, 4-methylpiperazino, etc.] and all stereoisomers, protected derivs., and salts were prepd. Techniques of combinatorial chem. can be applied to immobilized alkoxyamines to generate a diverse set of compds. Thus, (S,S)-HONHCOCH2CH(CH2CH2SMe)CONHCH(Bu-i)CONHC6H4NO2-p was prepd. and assayed for peptide **deformylase** and antimicrobial activities [IC50 = 11 nM and 64 .mu.M/mL (S. **aureus**), resp.].

L16 ANSWER 26 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:499918 BIOSIS
DOCUMENT NUMBER: PREV200000500039
TITLE: Resistance to **deformylase** inhibitor VRC483 is caused by mutations in formyl transferase.
AUTHOR(S): Margolis, P. (1); Hackbarth, C. (1); Lopez, S. (1); White, R. (1); Trias, J. (1)
CORPORATE SOURCE: (1) Versicor, Inc., Fremont, CA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (1999) Vol. 39, pp. 334. cd-rom. Meeting Info.: 39th Interscience Conference on

Antimicrobial Agents and Chemotherapy San Francisco, California, USA September 26-29, 1999 American Society for Microbiology
.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L16 ANSWER 27 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:499923 BIOSIS
DOCUMENT NUMBER: PREV200000500044
TITLE: VRC483, a naturally occurring antibacterial agent, is a potent **deformylase** inhibitor.
AUTHOR(S): Chen, D. (1); Patel, D. (1); Wu, C. (1); Young, D. (1); Hackbarth, C. (1); Wang, W. (1); Trias, J. (1); Ni, Z. (1); Lam, S. (1); White, R. (1); Yuan, Z. (1)
CORPORATE SOURCE: (1) Versicor, Inc., Fremont, CA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (1999) Vol. 39, pp. 333. cd-rom. Meeting Info.: 39th Interscience Conference on Antimicrobial Agents and Chemotherapy San Francisco, California, USA September 26-29, 1999 American Society for Microbiology
.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L16 ANSWER 28 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:499539 BIOSIS
DOCUMENT NUMBER: PREV200000499660
TITLE: Peptide **deformylase** as a target for discovery of novel antibacterial agent.
AUTHOR(S): Margolis, P. (1); Young, D. (1); Yuan, Z. (1); Wang, W. (1); Trias, J. (1)
CORPORATE SOURCE: (1) Versicor, Inc., Fremont, CA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (1999) Vol. 39, pp. 332. cd-rom. Meeting Info.: 39th Interscience Conference on Antimicrobial Agents and Chemotherapy San Francisco, California, USA September 26-29, 1999 American Society for Microbiology
.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

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